14 Colorectal cancer

Burden, epidemiology and priority interventions

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Colorectal cancer consists of cancer of the colon and the rectum and accounts for approximately 10% of new cancers globally.[1] The lifetime risk of developing colorectal cancer is as high as 4.3% in men and 4.0% in women.[2] As colorectal cancer is quite strongly associated with several of the NCD risk factors described in this book, there is significant potential for prevention. In addition, several screening tests are available and early treatment has a high rate of success.

Disease burden

According to IHME, colorectal cancer accounted for 1.9% (approximately 1.1 million) of all deaths worldwide in 2019 (increasing from 1.1% [0.52 million] in 1990), partly owing to growing and aging populations. Table 14.1 shows that the age-adjusted mortality rates of colorectal cancer decreased between 1990 and 2019 in high-income countries (HICs) but have otherwise slightly increased.

Globally, the total number of persons developing colorectal cancer is expected to rise in the decades ahead and colorectal cancer is expected to become the most common cancer by 2070, with 4.7 million new cases per year.[3] The increasing incidence will be largely driven by the increasing and aging populations, particularly in low- and middle-income countries, and by the increasing prevalence of some of the modifiable risk factors described below. Conversely, the incidence of colorectal cancer is expected to level off or even continue to decrease in HICs, given the stable age structure of the population, public health efforts to reduce exposures to modifiable risk factors, screening programmes and access to treatment. This, however, needs to be tempered with recent evidence of increasing rates of colorectal cancer in younger adults, possibly caused by changes in, or interactions between, diet, sedentary lifestyles and the rising prevalence of obesity.[4]

Risk and preventive factors

The aetiology of colorectal cancer is multifactorial. Around 70–75% of colorectal cancer occurs sporadically and is associated with modifiable risk factors.[5] The

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Table 14.1 Mortality for colorectal cancer (IHME)

	Global		*HICs*		*Upper MICs*		*Lower MICs*		*LICs*	
	1990	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*
Proportion of all deaths (%)	1.1	1.9	3.2	3.8	1.1	2.3	0.4	1.0	0.2	0.5
Age-standardized mortality rates (per 100,000)	14	14	21	17	12	14	8	10	7	8

main non-modifiable risk factors include male gender, older age and heritability.[6] As the two most common forms of hereditary colorectal cancer (hereditary non-polyposis colon cancer and familial adenomatous polyposis coli) only account for <5% of all colorectal cancer, there remains much to be understood on the interplay between genetics and the modifiable risk factors described below.[7]

Modifiable risk factors include high consumption of processed food (e.g. processed meat, a diet low in whole grain), alcohol, low physical activity, tobacco use and obesity. Protective factors include a diet high in whole grains, dietary fibre and calcium (e.g. from dairy products or calcium supplements) and regular physical activity.[4] There is reasonable evidence that non-starchy vegetables and fruits, and foods containing vitamins C and D, have a protective effect. According to IHME estimates in 2019, 51% of deaths from colorectal cancer were attributable to behavioural risk factors, including 33% due to unhealthy diet, 13% to tobacco use, 9% to alcohol, 8% to high body mass index (BMI) and 5% to low physical activity (note: the sum of the attributable fractions estimated separately for each risk factor exceeds the attributable fraction for all as the effects of risk factors are not independent of each other). The relationship between colorectal cancer and the composition of microorganisms in the gut (microbiota) is an area of considerable research, which may have preventive and treatment implications in the future.[8] Differences in the prevalence of risk factors and provision of health care between countries and over time mean that age-standardized rates of both incidence and mortality for colorectal cancer can vary by up to ten-fold across countries.[9]

Long-term use of low-dose non-steroidal anti-inflammatory drugs, including aspirin or ibuprofen (which inhibit the enzyme COX-2) is also associated with a reduced incidence and mortality of colorectal cancer and pre-malignant adenomas (relative risk 0.6–0.8), possibly by reducing the risk of colorectal cancers that overexpress COX-2, but not the risk of colorectal cancers with a weak or absent expression of COX-2.[10]

Interventions at the population level

The strong association of colorectal cancer with the modifiable risk factors described above emphasizes the importance of many of the WHO best buys

or recommended interventions that make an impact across the full range of NCDs described in several chapters in this book.

Screening

Colorectal cancer is preceded by pre-cancerous lesions (polyps), which can be identified during colonoscopy, biopsied and for smaller lesions removed at the same time. This has important implications when designing screening services/programmes and choosing which tests to use in these programmes. In order to be effective, population-based screening programmes should be implemented in a stepwise manner (including starting with a pilot phase), aim at high coverage of the target population, and be based on quality screening tests and treatment services.[11] Most experience with screening programmes has been in HICs.[12]

Screening tests. Most screening programmes use stool-based testing based on a faecal occult blood test (FOBT) or a faecal immunochemical test (FIT), with programmes increasingly moving from the inexpensive but less accurate FOBT to the more sensitive and reliable FIT. A positive screening test requires follow-up with colonoscopy or flexible sigmoidoscopy. A small number of screening programmes use flexible sigmoidoscopy or colonoscopy as a screening rather than a diagnostic tool. This has the advantage of allowing biopsies of suspected malignant or potentially malignant lesions (e.g. polyps that have evolved or are likely to evolve into cancer) to be removed at the time of screening. Other screening tools include direct visualization tests (e.g. computed tomography colonography), multi-target stool DNA tests, serum-based DNA tests (e.g. methylated septin 9 genes) and urine-based (metabolomic) tests, but they are not currently used for routine population-based screening. Despite the opportunities provided by screening, uptake is often suboptimal.[13] Screening programmes provide the opportunity for improving the health literacy of participants on options for the prevention and control of colon and other cancers.

Age and frequency of screening. The optimal age range target of a screening programme maximizes cost-effectiveness and will therefore vary between countries depending on the incidence of disease, health care capacity and competing priorities. Most screening programmes target individuals aged between 50 and 74 years, but the United States Preventive Services Task Force has recently recommended that the starting age for screening be reduced from 50 to 45 years. Other programmes, such as the one in the UK, start screening at the age of 60 years.[14] FOBT and FITs are usually undertaken annually or every two years. Computed tomography colonography and flexible sigmoidoscopy are conducted less frequently, typically every five years and every ten years for colonoscopy. For people over the age of 75 years, the decision to be screened should be based on resources available as well as the preferences of the individual and their life expectancy, overall health and prior screening history.

A recent review of colorectal cancer screening recommendations across the world identified 15 guidelines (six published in North America, six in Europe,

four in Asia and one from the World Gastroenterology Organization). The majority of guidelines recommend screening average-risk individuals between the ages of 50 and 75, using colonoscopy (every 10 years), flexible sigmoidoscopy (every 5 years) or FOBT, mainly FIT (annually or biennially). There are disparities throughout the different guidelines relating to the use of colonoscopy, rank order between tests, screening intervals and optimal age ranges for screening.[15] Population-based colorectal cancer screening, at age >50 years, linked with timely treatment is an intervention recommended by the WHO Global NCD Action Plan.

Resources for population-based screening programmes. Colorectal cancer screening programmes require significant resources for testing large numbers of people and ensuring adequate and timely follow-up of individuals with a positive test, particularly when compared with the greater frequency of other diseases (including NCDs) that could be prevented and treated more cost-effectively and/or more affordably.[16] Screening programmes require sustainable availability of diagnostic procedures (including quality clinical services for undertaking colonoscopy or flexible sigmoidoscopy and histopathology services) and availability of timely treatment (i.e. surgery and/or chemotherapy for cancer cases as well as surgery for the (infrequent) complications of colonoscopy). As a result, well-organized population-based screening programmes, even if cost-effective, may not be affordable and/or not of sufficient priority in a number of countries. Nevertheless, the increasing incidence of colorectal cancer in many low- and middle-income countries means that population screening programmes are likely to become more widespread in the coming years.[17] As with other population-based screening programmes, once established, it is often very difficult to discontinue a programme.

Opportunistic screening for high risk individuals. The priority here is to screen the first-degree relatives of those with a strong family history of colorectal cancer, including, where possible, the determination of a genetic cause. This should be done from the age of 18 years of age at regular intervals, provided resources are available for diagnosis, treatment and follow-up.

Treatment

Preventive treatment. Low-dose non-steroidal anti-inflammatory medications and/or aspirin may be considered in individuals with hereditary colorectal cancer syndromes, as this reduces the overall risk of colorectal cancer.[18]

Early-stage colorectal cancer (so-called 'cancerous polyps') can be removed by colonoscopy and usually requires no further treatment.

Colon cancer. Patients with colon cancer that has not spread to distant sites (most frequently the lungs and the liver) usually have surgery. Where lymph nodes are involved or there is a distant spread, chemotherapy (called adjuvant chemotherapy) is given for around 3–6 months after surgery. The type and duration of chemotherapy depend on the histological cancer type, age and comorbidities of the patient. Where resources permit, microsatellite

instability (MSI) in tumour cells should be determined to guide treatment and prognosis.

Rectal cancer. Patients with rectal cancer need often a multi-disciplinary approach including neoadjuvant (before surgery) chemo- and/or radiotherapy to decrease the size of the tumour (making surgery easier, including reducing the chance of having to operate on the anal sphincter, which is a high-risk procedure) and reduce the likelihood of local recurrence. Rectal cancer treatment is however centralized, in many countries, in experienced high-volume centres. Discussion in multidisciplinary tumour boards is crucial to personalize treatment for rectal cancer. If a patient has an excellent response to neoadjuvant treatment and presents a complete clinical response with no visible cancer, an expectative approach without surgery is possible in selected patients.

Follow-up. Patients should be followed up for five years to monitor for recurrence (which can occur in up to 50% of patients) in order to allow for early re-intervention. There is insufficient evidence to give aspirin to patients post-surgery.

Survival. In optimal settings, five-year survival after treatment for colorectal cancer may be as high as 95% for stage I, 85% for stage II, but only 70% for stage III and below 20% for stage IV.[19] MSI is a predictor of a better outcome.[20] Treatment of colorectal cancer stages I and II with surgery +/- chemotherapy and radiotherapy are therefore included as an effective intervention in the WHO Global NCD Action Plan.

Palliative care. Basic palliative care for cancer is a WHO effective intervention, including home-based and hospital care with multi-disciplinary teams and access to opiates and essential supportive medicines.

Monitoring

A comprehensive health information system that can provide ongoing routine quality data is important to develop and evaluate locally-tailored preventive and treatment programmes for colorectal cancer, track set targets and assess service provision, including across socio-economic and other relevant population sub-groups.

When resources allow, population-based cancer registries enable the collection of standardized data (e.g. cancer staging, accurate diagnosis and histology, survival time from diagnosis) that are required to track age-specific incidence and mortality as well as the impact of preventive and screening programmes.

Notes

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